REMARKS

Claims 1-6 stand rejected. No claim amendments have been made.

Applicant would like to thank the Examiner for the courtesy of an interview, held October 20, 2005.

Nonstatutory Double Patenting

Claims 1 through 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over copending Application No.: 10/624,746. In addition, claims 1 through 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over copening Application No.: 10/624,823 in combination with U.S. Patent Nos. 5,437,999 and 5,433,710. These rejections are *provisional* since the co-pending applications have not yet been allowed. Should the Examiner withdraw all pending rejections with the exception of the provisional double patenting rejections, Applicant will file a terminal disclaimer.

Claims 1 through 6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,284,125 in view of U.S. Patent Application No.: 5,437,999. Enclosed herewith is a terminal disclaimer. As such, Applicant respectfully requests withdrawal of this rejection.

Claim Rejection – 35 U.S.C. §103(a)

Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,437,999 to Diebold et al. ("Diebold") in view of U.S. Patent No. 5,089,320 to Straus et al. ("Straus"). The Examiner argues that Diebold discloses the limitations of claim 1, with the exception of a working electrode and a counter or counter/reference electrode spaced from about 20 microns to about 200 microns and an effective cell volume less than 1.5 microliters.
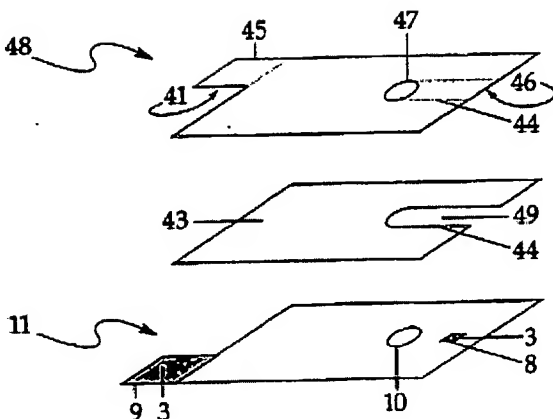
To remedy this deficiency that Examiner argues (1) that it would be possible to size the spacer between the electrodes in Diebold such that the electrode spacing of Diebold would fall

within the claimed range and (2) that varying the electrode spacing of Diebold, such that Diebold would fall within the claimed range, is obvious.
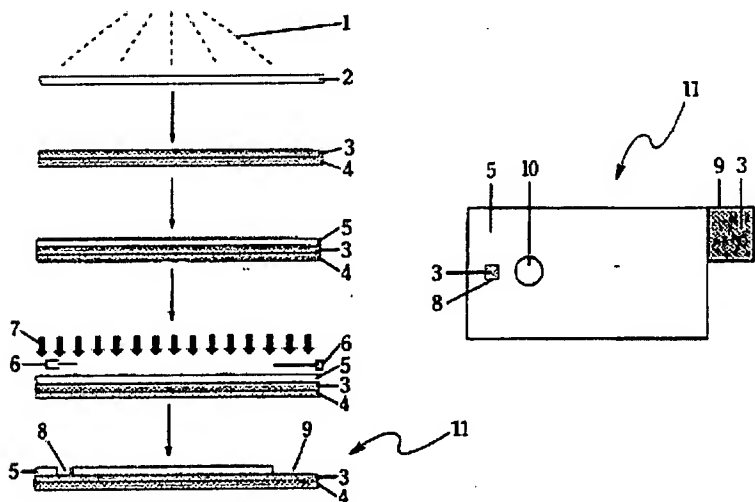
Applicant respectfully disagrees. As explained below, based on the structure of Diebold's device, it is clear that the electrode spacing of Diebold falls outside the claimed range. Furthermore, the choice of electrode spacing is not a simple matter of scale, as suggested by the Examiner, but rather the distance between the electrodes affects the manner in which the electrochemical cell functions. Thus, it is improper to attempt to re-size Diebold's device such that it reads on claim 1.

The claimed device is a device for measuring a concentration of an analyte (i.e., glucose) in a blood sample. The device includes at least one non-metal working electrode and at least one counter or counter/reference electrode, wherein the working and counter or counter/reference electrode are not coplanar and are separated by a distance of from about 20 microns to about 200 microns. A spacer is disposed between the electrodes and comprises a nonconductive polymeric material. The device includes a fluid permeable side-wall on at least one side of the hollow cell permitting entry of a sample into the hollow cell. The cell has an effective volume of less than 1.5 microliters. The device further includes means for applying an electrical potential difference between the working and counter or counter/reference and means for measuring a current between the working electrode and the counter or counter/reference electrode.

As mentioned above, nowhere does Diebold teach or disclose a device with the claimed electrode spacing or the claimed cell volume. Instead, Diebold discloses a device that includes a reference or counter electrode element (48) spaced form a working electrode element (11) by a spacer (43). FIG. 5, Col. 8, lines 15-20. FIGS 5 and 6 of Diebold are reproduced below.

Each electrode element (11, 48) is a multi-layered structure fabricated as illustrated in FIGS. 1 through 4. FIG. 1 of Diebold showing electrode element 11 is reproduced below.

Electrode element 11 includes an insulating substrate (4), a metalized layer (3), and a second insulating substrate (5). The exposed portion (8) of the metalized layer defines Diebold's

electrode. Electrode element 48 has a similar construction including two insulating layers with a metalized layer disposed therebetween.

Diebold fails to disclose electrode spacing, the thickness of the electrode elements (11, 48), or the spacing layer (43). The Examiner notes this fact, but points to the description of the exemplary material used to form the spacer layer; Mylar. The Examiner further notes that one of the outer layers of the electrode elements (i.e. the first insulating substrate) can be formed of Mylar having a thickness of approximately 10 mils. Based only on this use of common materials, the Examiner suggests that the Mylar spacer layer could have a similar thickness.

Applicant disagrees.

Diebold's device is formed from multiple layers, each have different functions and different required properties. The thickness of the outer layer of Diebold's device is a function of the structural supported needed to form the electrode element. Conversely, the spacer layer is based on the spacing of the electrode elements and effects the operation of the cell. Thus, the fact that the outer layer of Diebold's device can have a 10 mil thickness does not in any way suggest that the spacer should have a similar thickness. The layers perform different function and the mere use of similar materials does not in any way suggest that these layers could be substituted for one another.

Moreover, even if the substitution were proper (which it is not), the resulting device would have an electrode spacing above the claimed range. The 10 mil thickness of the outer layer is 254 microns. Thus, even if substituted, the spacer would be greater than the explicit range of 20 to 200 microns.

More importantly, Diebold's device includes more than just the spacer layer between electrodes. Each of the electrode elements (11, 48) includes a second insulating layer that will further space the Diebold's electrodes. Specifically, Diebold's electrodes are spaced by (1) the spacing layer "43" of unknown dimensions (although the Examiner argues 254 microns), (2) a second insulating layer "5", and (3) a second insulating layer "34." These three layers space Diebold's electrodes by far more than the claimed 20 to 200 micron range. Thus, given the large

electrode spacing found in Diebold, and the lack of any disclosure concerning cell volume, Diebold fails to teach or disclose the claimed invention.

In an attempt to overcome the failure of Diebold to suggest a device having the claimed limitations, the Examiner further argues that it even if Diebold falls far outside the claimed spacing and volume ranges it would have been *per se* obvious to scale Diebold's device such that it falls within the claimed range.

Applicant disagrees.

The Examiner cannot simply adjust the size of Diebold's device to meet the limitations of Applicant's claimed invention. Such a change would be based on impermissible hindsight gleamed from Applicant's own disclosure. Diebold's device, and other conventional devices at the time of Applicant's filing, function in a different way and thus such "scaling" is impermissible without some motivation.

Prior to the invention claimed in this application, it was believed that electrodes in an electrochemical cell must be spaced such that the reaction products from one electrode would not diffuse to the other electrode. Electrochemical cells were built according to this belief because they used the Cottrell equation to electrochemically analyze a sample. One of the underlying assumptions of the Cottrell analysis was that the electrodes were sufficiently spaced. If such spacing was not present, the analysis would produce inaccurate results.

Cottrell analysis is described in "Electrochemical Methods Fundamentals and Applications, 2nd Edition" Allen J. Bard and Larry R. Faulkner, pp. 161-64, John Wiley & Sons 2001 (copy of the cited pages enclosed). In particular, the book discusses the Cottrell equation and that it requires a "semi-infinite condition." This means that the processes occurring around the electrode are not disturbed by anything else, such as the processes at the counter electrode or convention or stirring, so the solution can be assumed to be of the same starting composition far away from the electrode and only perturbed by the diffusion caused by the electrochemistry going on at the working electrode.

An example of Cottrell analysis and the required spacing is found in a patent filed at the same time as the Diebold patent by the same Applicant as the Diebold patent. In particular, U.S.

Patent No.: 5,508,171 to Walling et al. ("Walling") discloses an assay method for use in an electrochemical cell. Walling states that "[e]lectrodes 4 and 5 must be sufficiently separated so that the electrochemical events at one electrode do not interfere with the electrochemical events at the other electrode. The preferred distance between electrodes 4 and 5 is about 1.2 millimeters." Col. 3, lines 43-47.

Other exemplary references from this time period which rely on the Cottrell equation, and thus minimum electrode spacing, include U.S. Patent No. 5,108,564 to Szuminsky et al., FIG. 8, Col. 3, lines 49-53; and U.S. Patent No. 5,243,516 to White, Col 1, line 65 to Col. 2, line 65; and U.S. Patent No. 5,916,156 to Hildenbrand et al., Col. 2, lines 11-35.[1]

Conversely, Applicant's electrode spacing allows for the reaction products at one electrode to diffuse to the other electrode, thus the minimal spacing required in claim 1. Applicant has found that the diffusion of species between electrodes can be accounted for using a different analytical technique. Thus, adjusting the spacing of Diebold's electrodes is not a simple matter of scaling, but rather results in device that functions differently (i.e., a device in which reaction products can diffuse across the cell).

Since Applicant's device function differently due to the claimed electrode spacing, the Examiner must point to some motivation to adjust the electrode spacing and cell volume of Diebold. However, such motivation is lacking. The Examiner has failed to point to any reason why one of ordinary skill in the art would adjust the electrode spacing and cell volume of Diebold to match those claimed by Applicant. The lone statement in Diebold that a "very small sample size" is intended does not suggest that electrodes should be spaced in the range of about 20 to 200 microns. Diebold is most likely referring to the relative size of the disclosed planar cell compared to large, bench top electrochemical cells (i.e., jar with electrodes). Planar electrochemical cells are certainly very small in comparison. Thus, given the limitations of the Cottrell equation, one skilled in the art would not have motivation to construct an electrochemical cell as claimed by Applicant.

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[1] The fact that Diebold lacks any disclosure regarding electrode spacing suggests that Diebold's electrodes are spaced by more then 200 microns. If Diebold's electrodes were intended to be spaced so closely, it would have been notable and surely the Diebold Applicant would have commented on such a distinction from the prior art.

Moreover, one skilled in the art would not have a reasonable expectation of success since Applicant's electrode spacing would not allow the use of the Cottrell equation. Faced with the suggestion to reduce electrode spacing, one skilled in the art would believe that the device could function accurately.

Without the necessary motivation and some reasonable expectation of success, Diebold's device cannot simply be "scaled" such that the electrode spacing matches the claimed range. The Examiner has thus failed to present a prima facie case of obviousness based on the disclosure of Diebold.

The Straus Reference

The Examiner cited the Straus reference to show that thin Mylar layers were known at the time of Applicant's filing. Straus discloses a resealable packaging material composed of several layers laminated together. One of the layers can be Mylar and have a variety of thicknesses including 12.2 and 25 microns. However, the use of Mylar in Diebold's disclosure and the fact that thin Mylar layers were used in composite packaging materials does not in anyway suggest that the Mylar layer of Straus should (or could) be substituted into the device of Diebold. Moreover, Straus is directed to a completely different use of Mylar, specifically resealable packaging material Thus, the Straus reference fails to provide any motivation for spacing electrodes according to Applicant's invention.

Accordingly, Applicant requests withdrawal of the rejection of claims 1, and the claims which depend therefrom, based on the combination of Diebold and Straus.

The rejection of Claim 5

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,437,999 to Diebold et al. ("Diebold") in view of U.S. Patent No. 5,089,320 to Straus et al. ("Straus"), and further in view of U.S. Patent No. 5,126,034 to Carter et al. ("Carter") and U.S. Patent No. 5,399,256 to Bohs ("Bohs"). Carter and Bohs are cited to teach the combination of a non-metal (carbon) working electrode and a silver counter/reference electrode. However, as discussed above, Diebold and Straus fail to disclose the limitation of independent claim 1. In addition, neither Carter nor Bohs suggest an electrochemical cell having electrode spacing in the

range of about 20 to 200 microns or a cell volume of less than 1.5 microliters. Accordingly, Applicant resepectfully requests withdrawal of the rejection of claim 6 in view of Diebold, Straus, Carter, and Bohs.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Please feel free to contact the undersigned should any issues remain unresolved.

Dated: December 28, 2005

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(c) Reversible (Nernstian) Electrode Process

For very rapid electrode kinetics, we have seen that the *i-E* relation collapses generally to a relation of the Nernst form (Sections 3.4.5 and 3.5.3):

$$E = E^{0'} + \frac{RT}{nF} \ln \frac{C_O(0, t)}{C_R(0, t)} \tag{5.1.5}$$

Again the kinetic parameters k^0 and α are not involved, and mathematical treatments are nearly always greatly simplified.

(d) Totally Irreversible Electron Transfer

When the electrode kinetics are very sluggish (k^0 is very small), the anodic and cathodic terms of (5.1.3) are never simultaneously significant. That is, when an appreciable net cathodic current is flowing, the second term in (5.1.3) has a negligibly small effect, and vice versa. To observe the net current, the forward process must be so strongly activated (by application of an overpotential) that the back reaction is virtually totally inhibited. In such cases, observations are always made in the "Tafel region," hence one of the terms in (5.1.3) can be neglected (see also Sections 3.4.3 and 3.5.4).

(e) Quasireversible Systems

Unfortunately, electrode processes are not always facile or very sluggish, and we sometimes must consider the whole *i-E* characteristic. In such *quasireversible (or quasi-nernstian* cases), we recognize that the net current involves appreciable activated components from the forward and reverse charge transfers.

In delineating these special situations, we are mostly concentrating on electrode processes that are chemically reversible; however the mechanism of an electrode process often involves an irreversible chemical transformation, such as the decay of the electron-transfer product by a following homogeneous reaction. A good specific example features anthracene in DMF, which we have already considered previously. If a proton donor, such as water, is present in the solvent, the anthracene anion radical is protonated irreversibly and several other steps follow, eventually yielding 9,10-dihydroanthracene. Treating any case in which irreversible chemical steps are linked to heterogeneous electron transfer is much more complicated than dealing with the heterogeneous electron transfer alone. One of the simplified cases, given in (a)–(d) earlier might apply to the electron-transfer step, but the homogeneous kinetics must also be added into the picture. Even in the absence of coupled-solution chemistry, chemically reversible electrode processes can be complicated by multistep heterogeneous electron transfer to a single species. For example, the two-electron reduction of Sn^{4+} to Sn^{2+} can be treated and understood as a sequence of one-electron transfers. In Chapter 12, we will see how more complicated electrode reactions like these can be handled.

POTENTIAL STEP UNDER DIFFUSION CONTROL

Planar Electrode

Previously, we considered an experiment involving an instantaneous change in potential from a value where no electrolysis occurs to a value in the mass-transfer-controlled region for reduction of anthracene, and we were able to grasp the current-time response qualitatively. Here we will develop a quantitative treatment of such an experiment. A planar electrode (e.g., a platinum disk) and an unstirred solution are presumed. In place of the

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anthracene example, we can consider the general reaction $O + ne \rightarrow R$. Regardless of whether the kinetics of this process are basically facile or sluggish, they can be activated by a sufficiently negative potential (unless the solvent or supporting electrolyte is reduced first), so that the surface concentration of O becomes effectively zero. This condition will then hold at any more extreme potential. We will consider our instantaneous step to terminate in this region.

(a) Solution of the Diffusion Equation

The calculation of the diffusion-limited current, i_d, and the concentration profile, $C_O(x, t)$, involves the solution of the linear diffusion equation:

$$\frac{\partial C_O(x, t)}{\partial t} = D_O \frac{\partial^2 C_O(x, t)}{\partial x^2} \tag{5.2.1}$$

under the boundary conditions:

$$C_O(x, 0) = C_O^* \tag{5.2.2}$$

$$\lim_{x \to \infty} C_O(x, t) = C_O^* \tag{5.2.3}$$

$$C_O(0, t) = 0 \quad \text{(for } t > 0) \tag{5.2.4}$$

The *initial condition*, (5.2.2), merely expresses the homogeneity of the solution before the experiment starts at $t = 0$, and the *semi-infinite condition*, (5.2.3), is an assertion that regions distant from the electrode are unperturbed by the experiment. The third condition, (5.2.4), expresses the condition at the electrode surface after the potential transition, and it embodies the particular experiment we have at hand.

Section A.1.6 demonstrates that after Laplace transformation of (5.2.1), the application of conditions (5.2.2) and (5.2.3) yields

$$\overline{C}_O(x, s) = \frac{C_O^*}{s} + A(s)\, e^{-\sqrt{s/D_O}\,x} \tag{5.2.5}$$

By applying the third condition, (5.2.4), the function $A(s)$ can be evaluated, and then $\overline{C}_O(x, s)$ can be inverted to obtain the concentration profile for species O. Transforming (5.2.4) gives

$$\overline{C}_O(0, s) = 0 \tag{5.2.6}$$

which implies that

$$\overline{C}_O(x, s) = \frac{C_O^*}{s} - \frac{C_O^*}{s} e^{-\sqrt{s/D_O}\,x} \tag{5.2.7}$$

In Chapter 4, we saw that the flux at the electrode surface is proportional to the current; specifically,

$$-J_O(0, t) = \frac{i(t)}{nFA} = D_O \left[\frac{\partial C_O(x, t)}{\partial x}\right]_{x=0} \tag{5.2.8}$$

which is transformed to

$$\frac{\overline{i}(s)}{nFA} = D_O \left[\frac{\partial \overline{C}_O(x, s)}{\partial x}\right]_{x=0} \tag{5.2.9}$$

The derivative in (5.2.9) can be evaluated from (5.2.7). Substitution yields

$$\overline{i}(s) = \frac{nFAD_O^{1/2}C_O^*}{s^{1/2}} \tag{5.2.10}$$

and inversion produces the current-time response

$$i(t) = i_d(t) = \frac{nFAD_O^{1/2}C_O^*}{\pi^{1/2}t^{1/2}} \tag{5.2.11}$$

which is known as the *Cottrell equation* (3). Its validity was verified in detail by the classic experiments of Kolthoff and Laitinen, who measured or controlled all parameters (1, 2). Note that the effect of depleting the electroactive species near the surface leads to an inverse $t^{1/2}$ function. We will encounter this kind of time dependence frequently in other kinds of experiments. It is a mark of diffusive control over the rate of electrolysis.

In practical measurements of the *i-t* behavior under "Cottrell conditions" one must be aware of instrumental and experimental limitations:

1. *Potentiostatic limitations.* Equation 5.2.11 predicts very high currents at short times, but the actual maximum current may depend on the current and voltage output characteristics of the potentiostat (Chapter 15).

2. *Limitations in the recording device.* During the initial part of the current transient, the oscilloscope, transient recorder, or other recording device may be overdriven, and some time may be required for recovery, after which accurate readings can be displayed.

3. *Limitations imposed by R_u and C_d.* As shown in Section 1.2.4, a nonfaradaic current must also flow during a potential step. This current decays exponentially with a *cell time constant*, R_uC_d (where R_u is the uncompensated resistance and C_d is the double-layer capacitance). For a period of about five time constants, an appreciable contribution of charging current to the total measured current exists, and this superimposed signal can make it difficult to identify the faradaic current precisely. Actually, the charging of the double layer is the mechanism that establishes a change in potential; hence the cell time constant also defines the shortest time scale for carrying out a step experiment. The time during which data are collected after a step is applied must be much greater than R_uC_d if an experiment is to fulfill the assumption of a practically instantaneous change in surface concentration at $t = 0$ (see Sections 1.2.4 and 5.9.1).

4. *Limitations due to convection.* At longer times the buildup of density gradients and stray vibrations will cause convective disruption of the diffusion layer, and usually result in currents larger than those predicted by the Cottrell equation. The time for the onset of convective interference depends on the orientation of the electrode, the existence of a protective mantle around the electrode, and other factors (1, 2). In water and other fluid solvents, diffusion-based measurements for times longer than 300 s are difficult, and even measurements longer than 20 s may show some convective effects.

(b) Concentration Profile
Inversion of (5.2.7) yields

$$C_O(x, t) = C_O^*\left\{1 - \text{erfc}\left[\frac{x}{2(D_O t)^{1/2}}\right]\right\} \tag{5.2.12}$$

or

$$C_O(x, t) = C_O^* \, \text{erf}\left[\frac{x}{2(D_O t)^{1/2}}\right] \tag{5.2.13}$$

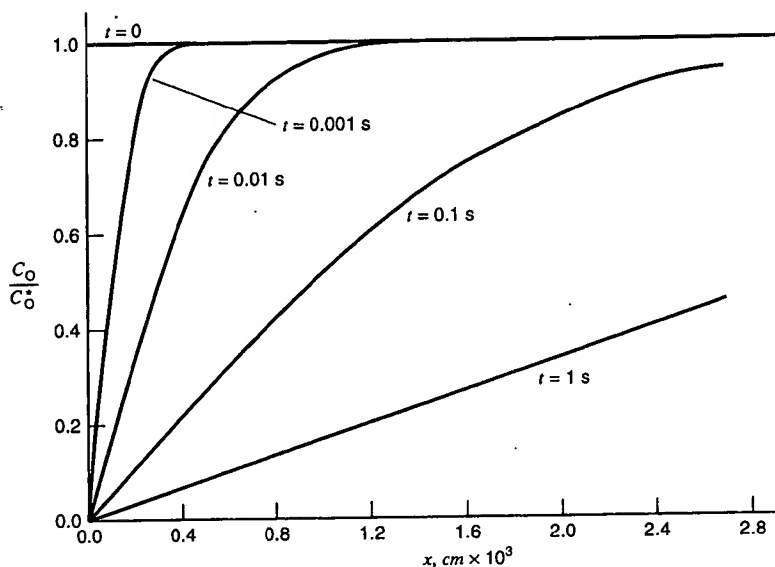**Figure 5.2.1** Concentration profiles for several times after the start of a Cottrell experiment. $D_O = 1 \times 10^{-5}$ cm^2/s.

Figure 5.2.1 comprises several plots from (5.2.13) for various values of time. The depletion of O near the electrode is easily seen, as is the time-dependent falloff in the concentration gradient at the electrode surface, which leads to the monotonically decreasing i_d function of (5.2.11).

One can also see from Figure 5.2.1 that the *diffusion layer*, that is the zone near the electrode where concentrations differ from those of the bulk, has no definite thickness. The concentration profiles asymptotically approach their bulk values. Still, it is useful to think about the thickness in terms of $(D_O t)^{1/2}$, which has units of length and characterizes the distance that species O can diffuse in time t. Note that the argument of the error function in (5.2.13) is the distance from the electrode expressed in units of $2(D_O t)^{1/2}$. The error function rises very rapidly toward its asymptote of 1 (see Section A.3). When its arguments are 1, 2, and 3 (i.e., when x is 2, 4, and 6 times $(D_O t)^{1/2}$), it has values, respectively, of 0.84, 0.995, and 0.99998; thus the diffusion layer is completely contained within a distance of $6(D_O t)^{1/2}$ from the electrode. For most purposes, one can think of it as being somewhat thinner. People often talk of a *diffusion layer thickness*, because there is a need to describe the reach of the electrode process into the solution. At distances much greater than the diffusion layer thickness, the electrode can have no appreciable effect on concentrations, and the reactant molecules there have no access to the electrode. At distances much smaller, the electrode process is powerfully dominant. Even though no consistent or accepted definition exists, people often define the thickness as 1, $2^{1/2}$, $\pi^{1/2}$, or 2 times $(D_O t)^{1/2}$. Any of these ideas suffices. We have already seen diffusion lengths defined in different ways in Sections 1.4.3 and 4.4.1.

Of course the thickness of the diffusion layer depends significantly on the time scale of the experiment, as one can see in Figure 5.2.1. For a species with a diffusion coefficient of 1×10^{-5} cm^2 s^{-1}, $(D_O t)^{1/2}$ is about 30 μm for an experimental time of 1 s, but only 1 μm at 1 ms, and just 30 nm at 1 μs.